

We Claim:

1. An implantable medical device comprising an implantable medical device having a coating on at least one portion of at least one surface, said coating comprising:  
an inner layer of a cationic polyelectrolyte carrier; and  
a layer of at least one negatively charged therapeutic agent adsorbed onto said inner layer of cationic polyelectrolyte carrier; and  
optionally, an additional layer or layers of cationic polyelectrolyte carrier and an additional layer or layers of at least one negatively charged therapeutic agent adsorbed onto said additional layer or layers of cationic polyelectrolyte carrier, wherein said additional layer or layers of polyelectrolyte carrier and said additional layer or layers of negatively charged therapeutic agent alternate.

2. The medical device of claim 1, further comprising an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner or additional layer or layers of cationic polyelectrolyte carrier.

3. The medical device of claim 2, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one inner or additional layer or layers of polyelectrolyte carrier.

4. The medical device of claim 1, wherein at least one inner or additional layer of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

5. The medical device of claim 1, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

6. The medical device of claim 1, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-

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thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

7. The medical device of claim 1, wherein at least one of the one or more therapeutic agent comprises rapamycin.
8. The medical device of claim 1, wherein at least one of the one or more therapeutic agent comprises paclitaxel.
9. The medical device of claim 1, wherein at least one of the one or more therapeutic agent comprises a polynucleotide encoding a therapeutic molecule, wherein said polynucleotide is inserted into an adenovirus vector.
  
10. A method of adsorbing a negatively charged therapeutic agent onto the surface of a medical device comprising:
  - (a) coating at least one portion of at least one surface of a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;
  - (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
  - (c) adsorbing one or more negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
  - (d) washing the layer of therapeutic agent with a washing solution and repeating steps

(a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

11. The method of claim 10, further comprising the step of coating the outermost layer of therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

12. The method of claim 11, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of polyelectrolyte carrier.

13. The method of claim 10, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

14. The method of claim 10, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

15. The method of claim 10, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

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16. The method of claim 10, wherein at least one of the one or more therapeutic agent comprises rapamycin.

17. The method of claim 10, wherein at least one of the one or more therapeutic agent comprises paclitaxel.

18. The method of claim 10, wherein at least one of the one or more therapeutic agent comprises a polynucleotide encoding a therapeutic molecule, wherein said polynucleotide is inserted into an adenovirus vector.

19. A medical device comprising a negatively charged therapeutic agent adsorbed on the surface thereof and produced by a process comprising:

- (a) coating at least one portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;
- (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (c) adsorbing one or more negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (d) washing the layer of therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

20. The medical device of claim 19, wherein the process further comprises the step of coating the outermost layer of therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

21. The method of claim 20, wherein the outermost layer of cationic polyelectrolyte carrier is

more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

22. The medical device of claim 19, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

<sup>19</sup> <sup>15</sup> 23. The medical device of claim 19, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

~~24. The medical device of claim 19, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, antimicrobials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.~~

25. The medical device of claim 19, wherein at least one of the one or more therapeutic agent comprises rapamycin.

26. The medical device of claim 19, wherein at least one of the one or more therapeutic agent comprises paclitaxel.

27. The medical device of claim 19, wherein at least one of the one or more therapeutic agent comprises a polynucleotide encoding a therapeutic molecule, wherein said polynucleotide is inserted into an adenovirus vector.

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28. A method of delivering a therapeutic agent to a target location by implanting in or near the target location a medical device comprising a negatively charged therapeutic agent adsorbed on the surface thereof, wherein the medical device is produced by a process comprising:

(a) coating at least one portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(b) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing one or more negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally

(d) washing the layer of therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

29. The method of claim 28, further comprising the step of coating the outermost layer of therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

30. The method of claim 29, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

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31. The method of claim 28, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

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32. The method of claim 28, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

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33. The method of claim 28, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

34. The method of claim 28, wherein at least one of the one or more therapeutic agent comprises rapamycin.

35. The method of claim 28, wherein at least one of the one or more therapeutic agent comprises paclitaxel.

36. The method of claim 28, wherein at least one of the one or more therapeutic agent comprises a polynucleotide encoding a therapeutic molecule, wherein said polynucleotide is inserted into an adenovirus vector.

37. The method of claim 28, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, urethra malignant growth, or benign growth.

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38. A method for treating or reducing the occurrence or severity of a clinical disease or condition, comprising:

(a) preparing a medical device by:

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- (i) coating at least one portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing one or more negatively charged therapeutic agent effective to treat or reduce the occurrence of the clinical disease or condition onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into a target location from which the therapeutic agent can treat or reduce the occurrence or severity of the clinical disease or condition.

39. The method of claim 38, further comprising the step of coating the outermost layer of therapeutic agent with an outermost layer of cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

40. The method of claim 39, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

41. The method of claim 38, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a

combination thereof.

<sup>34</sup> <sup>30</sup> 42. The method of claim 38, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

~~43. The method of claim 38, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.~~

44. The method of claim 38, wherein the clinical disease or condition comprises restenosis or angiogenesis and at least one of the one or more therapeutic agent comprises rapamycin.

45. The method of claim 38, wherein the clinical disease or condition comprises a malignancy or malignant cell growth and at least one of the one or more therapeutic agent comprises paclitaxel.

<sup>513 A1</sup> 46. The method of claim 38, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, ovary, testes, malignant growth, or benign growth.

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